Correlation Between Diagnostic Imaging Findings of Sacroiliitis and Inflammation Parameters

Korrelation zwischen diagnostischer Bildgebung und Entzündungsparametern bei Sakroiliitis

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ABSTRACT

Objectives Sacroiliitis is an inflammation of the sacroiliac joints. Diagnostic imaging has a very important role in the diagnosis of sacroiliac involvement in the disease process. In addition, laboratory parameters can also be useful for the detection of inflammation. This study aims to investigate the relationship between active sacroiliitis and subclinical inflammation parameters in patients who underwent MRI and 99mTc-methylene diphosphonate (MDP) bone scintigraphy.

Material and Methods This study includes 65 patients with suspected spondyloarthritis (SpA). Patients who had a sacroiliac MRI, a 99mTc-MDP bone scintigraphy and a complete blood count (CBC) within 3 months were reviewed retrospectively. Sacroiliac joints were evaluated bilaterally by using bone scintigraphy and MRI. Blood inflammation parameters were further assessed regarding evidence of probable sacroiliitis.

Results Significant differences were reported between MRI groups for sacroiliac indices (SII) ($p = 0.003$), neutrophil-to-lymphocyte ratio (NLR) ($p = 0.008$), C-reactive protein (CRP) ($p = 0.037$), and white blood cell (WBC) count ($p = 0.031$). A significant correlation was found between active sacroiliitis and SII ($p = 0.001$), CRP ($p = 0.000$), erythrocyte sedimentation rate (ESR) ($p = 0.000$), and NLR ($p = 0.001$). Based on the ROC curve analysis, SII was found to have a sensitivity of 64.3 % and specificity of 69.8 %; NLR was found to have a sensitivity of 64.3 % and specificity of 73.3 % for diagnosing active sacroiliitis.

Conclusions Subclinical inflammation indices obtained from CBC and, particularly, NLR may contribute to disease activity assessment like acute-phase reactants. However, this needs to be confirmed in further studies.

ZUSAMMENFASSUNG

Hintergrund Die Sakroiliitis ist eine Entzündung der Iliosakralgelenke. Bei der Diagnose einer Beteiligung der Iliosakralgelenke am Krankheitsprozess spielt die diagnostische Bildgebung eine sehr wichtige Rolle. Darüber hinaus können auch Laborparameter zum Nachweis von Entzündungen nützlich sein. Ziel dieser Studie ist die Untersuchung der Beziehung zwischen aktiver Sakroiliitis und subklinischen Entzündungsparametern bei Patienten, bei denen eine MRT-Untersuchung und eine Knochenszintigrafie mit 99mTc-Methylendiphosphonat (MDP) durchgeführt wurde.

Material und Methoden In diese Studie wurden Patienten mit Sakroiliitis, bei denen eine MRT und eine Knochenszintigrafie mit 99mTc-MDP durchgeführt wurden und ein vollständiges Blutbild vorlag, innerhalb von 3 Monaten retrospektiv nachuntersucht. Es erfolgte eine bilaterale Beurteilung der Iliosakralgelenke mittels Knochenszintigrafie und MRT. Außerdem wurde anhand der Entzündungsparameter im Blut festgestellt, ob Hinweise auf eine Sakroiliitis vorlagen.

Ergebnisse Es fanden sich signifikante Unterschiede zwischen den MRT-Gruppen in Bezug auf iliosakrale Indizes (SII) (p = 0,003), Neutrophilen-Lymphozyten-Verhältnis (NLR) (p = 0,008), C-reaktives Protein (CRP) (p = 0,037) und Leukozytenzahl (p = 0,031). Eine signifikante Korrelation zeigte sich zwischen aktiver Sakroillitis und SII (p = 0,001), CRP (p = 0,000), Erythrozytensedimentationrate (ESR) (p = 0,000) und NLR (p = 0,001). Basierend auf der ROC-Kurvenanalyse wurden für SII zur Diagnose einer aktiven Sakroiliitis eine Sensitivität von 64,3 % und eine Spezifität von 69,8 % sowie für NLR eine Sensitivität von 64,3 % und eine Spezifität von 73,3 % ermittelt.
Schlussfolgerungen Subklinische Entzündungsindizes, die anhand des Blutbilds und insbesondere des NLR bestimmt werden, können wie Akutphasenreaktanten zur Beurteilung der Krankheitsaktivität beitragen. Dies muss jedoch durch weitere Studien bestätigt werden.

Introduction

Sacroiliitis is an inflammation of the sacroiliac joint. It is an important finding of axial spondyloarthritis (axSpA) and also can be seen in many other rheumatic and non-rheumatic diseases [1].

Clinical features include disabling, inflammatory low back pain and morning stiffness, which are not pathognomonic for sacroiliitis. Therefore, imaging has a very important role in the diagnosis of sacroiliac involvement in the disease process [2].

Since the early 1990s, magnetic resonance imaging (MRI) has been progressively used to detect inflammation in the sacroiliac joints and spine [3, 4]. Use of MRI has changed the diagnosis of SpA over the years [5]. MRI has been identified as the best method for detecting active sacroiliitis, especially at the early stages of the disease before radiographs able to detect structural damages. However, MRI is relatively expensive and not available everywhere [6, 7]. Also MRI can hardly be performed on occasions like claustrophobia, metallic implants, and implantable devices [8]. Radionuclide bone scintigraphy is still used for this purpose, and it has the ability to image entire skeleton and joints in terms of new bone formation with high sensitivity at a reasonable cost [7, 9]. After infusion, Tc-99 m MDP is immediately accumulated into the bone [9]. While the radiopharmaceutical retention is related to level of blood supply to the bone tissue, the accumulation of Tc-99 m MDP is mainly depends on osteoblastic activity [9]. Higher levels of Tc-99 m MDP are observed in areas with active bone development and repair than in mature bone tissue[9].

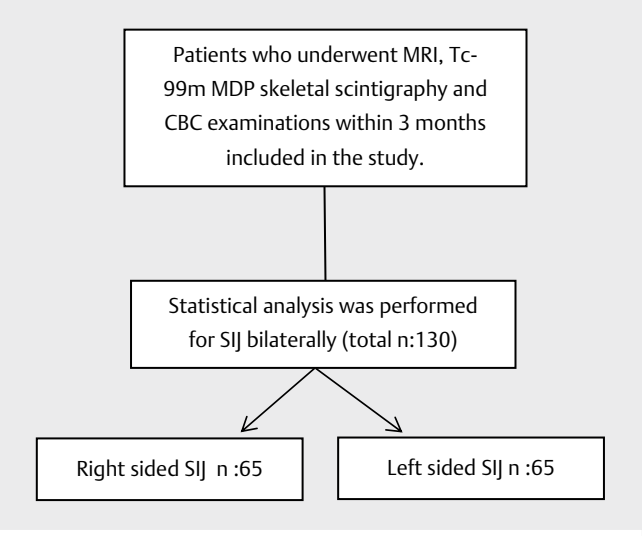
Additionally, laboratory parameters can also be useful for the detection of inflammation. An elevated acute-phase response may be present, including an elevated erythrocyte sedimentation rate and elevated C-reactive protein but a normal erythrocyte sedimentation rate and C reactive protein do not exclude axSpA or active disease. Acute-phase reactants have been playing a more prominent role in monitoring patients with axSpA in recent years than before. The Ankylosing Spondylitis Disease Activity Score (ASDAS) is the first validated disease activity score, which combines patient-reported outcomes and C reactive protein or erythrocyte sedimentation rate [6, 10]. In recent clinical studies, subclinical inflammatory parameters such as r have been found to be related with inflammation in diseases such as Familial Mediterranean Fever [11].

There are many studies examining the correlation between the clinical disease activity of sacroiliitis and subclinical inflammation parameters . According to the current literature, this is the first study that examines the relationship between the imaging findings of sacroiliitis (sacroiliac MRI and visual/quantitative analysis of 99mTc-MDP bone scintigraphy results) and subclinical inflammation parameters.

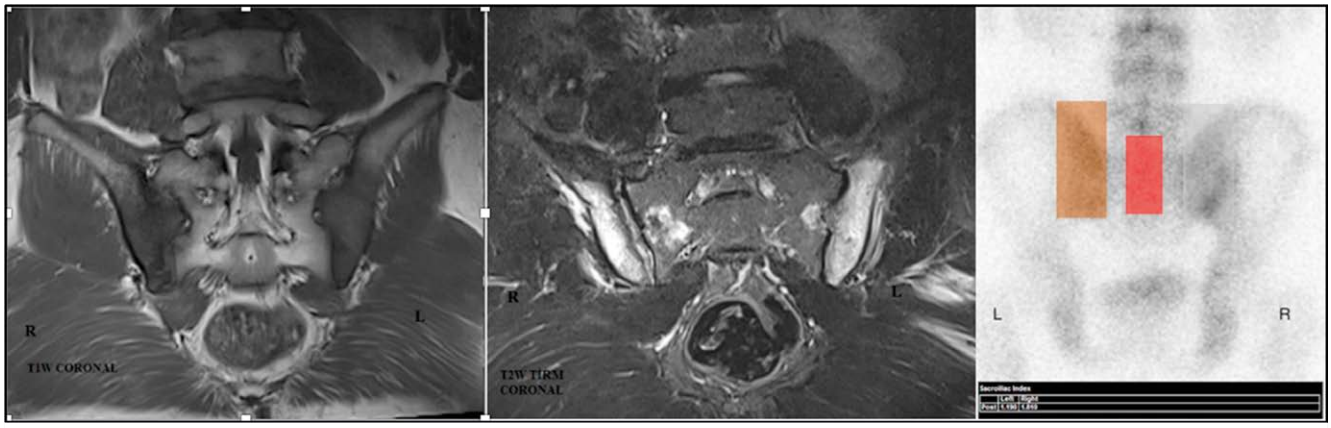
Methods

A total of 130 sacroiliac joints in 65 patients with suspected spondyloarthritis (SpA) and sacroiliitis were investigated in this retrospective, cross-sectional study. Sacroiliac joints were evaluated bilaterally by using both bone scintigraphy and MRI for the differential diagnosis of sacroiliitis. Patients who underwent sacroiliac MR, 99m Tc-MDP bone scintigraphy and complete blood count (CBC) in 3 months between 2015–2019 at Karabuk University Training and Research Hospital were included in this study. The patients whose sacroiliac MR and scintigraphic image qualities were not suitable for evaluation and patients who had more than 3 months between imaging and laboratory examinations were excluded from this study (▶ **Fig. 1**).

The sacroiliac joints were evaluated bilaterally by using 99mTc-MDP bone scintigraphy and MRI images (▶ **Fig. 2**). Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, platelet count, platelet distribution width, mean platelet value, white blood cell count, C reactive protein, erythrocyte sedimentation rate were further assessed whether indicating probable sacroiliitis.



▶ **Fig. 1** Flow chart of the study.



▶ **Fig. 2** Low signal intensity on T1W (Left) and high signal intensity on fat saturated T2W TIRM coronal MRI images (Middle) at right sacroiliac joint revealing bone marrow oedema. Peak counts obtained by rectangular ROI of both saroiliac joints and sacrum providing SII calculation (Right). Right and left SII is 1.81 and 1.19 respectively.

MRI studies were done using 1.5-T scanner (Magnetom Essenza, Siemens, Erlangen, Germany). The MRI examinations were performed with a torso coil and a spine coil consisted of the following sequences: coronal T1A-weighted turbo spin-echo, axial T2-weighted gradient-echo, T2 coronal turbo inversion recovery magnitude (TIRM), and contrast-enhanced T1-weighted fat-saturated images, if necessary. The presence of sacroiliitis were reported as bone marrow edema /osteitis for active sacroiliitis and subchondral sclerosis, erosions, periarticular fat deposition, bony bridges/ankylosis for structural damage (chronic sacroiliitis) on MRI reports. MRI reports were grouped as active sacroiliitis-positive (n = 14), active sacroiliitis negative (n = 116) by using Assessment of SpondyloArthritis International Society (ASAS) criteria [12].

Bone scintigraphy was performed using intravenous 600 MBq (megabecquerel) 99mTc-MDP, with a double-headed gamma camera equipped with a low-energy, high-resolution collimator (Mediso AnyScan S, Mediso Medical Imaging Systems Ltd., Budapest, Hungary). Anterior and posterior images of the pelvis were obtained using 256 × 256 matrix for 750,000 counts 3 hours after tracer injection. The presence of sacroiliitis were evaluated as visual and quantitative analysis using posterior static pelvis images by Interview XP software (Mediso Medical Imaging Systems Ltd., Budapest, Hungary). In quantitative analysis, rectangular regions of interest (ROIs) were drawn over both of the sacroiliac joints. A rectangular ROI was drawn over the adjacent sacral region. Sacroiliac joint indices (SII) (peak counts of sacroiliac joint ROI/peak counts of sacral ROI) was calculated for each joint. Scintigraphic visual findings grouped as sacroiliitis positive (n = 29), sacroiliitis negative (n = 101). The study was approved by local ethics committee (IRB No: 77192459–050.99-E.12903). .

Statistical analyses were performed using version 26.0 of SPSS software (IBM Corp., Armonk, NY, USA). Mean ± SD values were determined. The Kolmogorov–Smirnov test was used to compare groups and to determine whether the obtained parameters conformed to a normal distribution. The Mann–Whitney U test was used to evaluate differences between groups on variables. Point-biserial correlation was used to determine the relationship between dichotomous and continuous variables. The correlation coefficients and their significance were calculated using the Spearman test while investigating the associations between non-normally distributed continuous variables. The McNemar and kappa tests were used to compare agreement between MRI and scintigraphy modalities. The capacity of sacroiliac activity index and values of inflammation markers in predicting active sacroiliitis were analyzed using receiver operating characteristic (ROC) curve analyses. The sensitivity and specificity values were presented when a significant cut-off value was observed. The "cutoff" value was provided by combining the highest sensitivity and the highest specificity on the ROC curve based on detecting the highest point on the vertical axis and the furthest to the left on the horizontal axis [13].

While evaluating the area under the curve, a 5 % type 1 error level was used to accept a statistically significant predictive value of the test variables. A probability value of $p < 0.05$ was considered statistically significant.

Results

This study was completed with 130 sacroiliac joints in 65 patients. The mean age of the participants was 39.06 ± 14.38 years. Female and male participants in the study were 52.3 and 47.7 % respectively. As a result of MRI examinations, 70 sacroiliac joints were evaluated as sacroiliitis positive and 60 sacroiliac joints were detected as sacroiliitis negative. Among 70 sacroiliac joints; 14 sacroiliac joint were diagnosed as active (bone marrow edema/osteitis) sacroiliitis in 7 patients (n = 7 bilateral, n = 0 unilateral) and 56 sacroiliac joints as chronic phase sacroiliitis in 28 patients (n = 28 bilateral, n = unilateral). Patients' characteristics were shown in ▶ **Table 1**. Significant differences were reported between active sacroiliitis (bone marrow edema/osteitis) positive MRI group (n = 14) and active sacroiliitis negative group (n = 116) for sacroiliac joint indices (p = 0.003), neutrophil to lymphocyte ratio (p = 0.008), C reactive protein (p = 0.037), and white blood cell count (p = 0.031) (▶ **Table 2**). As a result of 99m Tc-MDP bone scintigraphy visual analysis, 29 sacroiliac joints were evaluated as sa-

▶ **Table 1** Patients' characteristics.

	Mean ± Standart Deviation
Age (years)	39.06 ± 14.08
Age of onset of symptoms	38.24 ± 1.74
Disease duration (month)	11.50 ± 1.59
Gender	n (%)
Female	34 (52.3%)
Male	31 (47.7%)
Diagnosis	n (%)
Axial Spondyloarthritis (axSpA) (Sacroiliitis positive)	35 (53.8%)
Lumbar Spondylosis (Sacroiliitis negative)	13 (20%)
Lumbar Disc Herniation (Sacroiliitis negative)	8 (12.3%)
Lumbar Strain (Sacroiliitis negative)	9 (13.9%)
HLA B27	n (%)
HLA B27 Positive	15 (23.1%)
HLA B27 Negative	50 (76.9%)
Sacroiliac Joint Involvement	n (%)
No Involvement	30 (46.2%)
Unilateral İnvolvement	0 (0%)
Bilateral Involvement	35 (53.8%)
Fulfilment of ASAS Classification Criteria	n (%)
Yes	35 (53.8%)
No	30 (46.2%)
Treatment of Patients	n (%)
Paracetamol	11 (16.9%)
Nonsteroidal anti-inflammatory drugs	42 (64.6%)
Disease modifying antirheumatic drugs (DMARD)	10 (15.4%)
Anti-tumor necrosis factor (Anti-TNF) drugs	2 (3.1%)

croiliitis positive and 101 sacroiliac joints were detected as sacroiliitis negative . A significant difference was observed between sacroiliitis positive (n = 29) and negative (n = 101) groups only with sacroiliac joint indices (p = 0.000) (▶ **Table 3**). Significant difference was observed between MRI and visual scintigraphic analysis in diagnosing active sacroiliitis (the McNemar test p = 0.003), and there was a weak agreement between them (p = 0.000, kappa = 0.374). Point-biserial test was used to analyze correlation between active sacroiliitis (bone marrow edema/osteitis) on MRI and inflammation markers and sacroiliac joint indices. A significant correlation was found between active sacroiliitis (bone marrow edema/osteitis) and sacroiliac joint indices (p = 0.001, r_{pb} = 0.298), C reactive protein (p = 0.000, r_{pb} = 0.439), erythrocyte sedimentation rate (p = 0.000, r_{pb} = 0.310), and neutrophil to lymphocyte ratio (p = 0.001, r_{pb} = 0.280). Point-biserial test was used to analyze correlation between sacroiliitis on visual bone scintigraphy analysis and inflammation markers and sacroiliac joint indices. Significant correlation was found between sacroiliitis on visual bone scintigraphy analysis only with sacroiliac indices (p < 0.000, r_{pb} = 0.433). The Spearman test was used to analyze correlation between inflammation markers and sacroiliac joint indices. A significant negative correlation was found between sacroiliac joint indices and platelet to lymphocyte ratio (p < 0.002, r = − 0.271); a significant positive correlation was found between sacroiliac joint indices and white blood cell count (p < 0.03, r = 0.190); and a significant correlation was found between neutrophil to lymphocyte ratio and C reactive protein (p = 0.019, r = 0.206), white blood cell count (p = 0.001, r = 0.293), platelet to lymphocyte ratio (p = 0.000, r = 0.505) and platelet distribution width (p = 0.022, r = 0.201) (▶ **Table 4**). Based on the ROC curve analysis, sacroiliac joint indices showed an area under curve of 0.746 (95% confidence interval [CI] = 0.635–0.858, p = 0.003); neutrophil to lymphocyte ratio showed an area under curve of 0.718 (95% CI = 0.546–0.890, p = 0.008); and C reactive protein showed an area under curve of 0.671 (95% CI = 0.503–0.838, p = 0.037) for diagnosing active (bone marrow edema/osteitis) sacroiliitis. Sacroiliac joint indices showed a sensitivity of 64.3% and specificity of 69.8% at a cut-off value of 1.297; neutro-

▶ **Table 2** Comparison of inflammation parameters between active sacroiliitis (bone marrow edema/osteitis) positive and negative groups on MRI.

	Active sacroiliitis positive group (bone marrow edema/osteitis) (Mean ± SD)	Active sacroiliitis negative group (Mean ± SD)	p-value
Sacroiliac joint indices	1.39 ± 0.07	1.16 ± 0.02	0.003
C reactive protein	18.94 ± 7.85	3.27 ± 0.35	0.037
Erithrocyte sedimentation rate	36.5 ± 7.74	20.14 ± 1.24	0.057
White blood cell count	8.07 ± 0.40	7.17 ± 0.15	0.031
Neutrophil to lymphocyte ratio	2.60 ± 0.25	1.89 ± 0.06	0.008
Platelet count	294.57 ± 23.02	272.24 ± 5.10	0.384
Platelet to lymphocyte ratio	141.32 ± 12.35	124.21 ± 3.34	0.129
Platelet distribution width	15.89 ± 0.12	15.28 ± 0.17	0.265
Mean platelet value	9.90 ± 0.39	9.93 ± 0.08	0.253

▶ **Table 3** Comparison of inflammation parameters between sacroiliitis positive and negative groups on visual analysis of 99m Tc-MDP bone scintigraphy.

	Sacroiliitis positive group (Mean ± SD)	Sacroiliitis negative group (Mean ± SD)	p-value
Sacroiliac joint indices	1.38 ± 0.04	1.13 ± 0.02	0.000
C reactive protein	4.60 ± 1.69	5.06 ± 1.16	0.053
Erithrocyte sedimentation rate	24.19 ± 4.17	21.25 ± 1.42	0.634
White blood cell count	7.24 ± 0.31	7.28 ± 0.16	0.767
Neutrophil to lymphocyte ratio	1.88 ± 0.14	1.99 ± 0.07	0.325
Platelet count	275.48 ± 11.20	274.41 ± 5.80	0.502
Platelet to lymphocyte ratio	120.55 ± 5.88	127.64 ± 3.87	0.440
Platelet distribution width	14.99 ± 0.41	15.44 ± 0.15	0.228
Mean platelet value	10.14 ± 0.22	9.87 ± 0.09	0.367

▶ **Table 4** Correlation between subclinical inflammation markers and sacroiliac joint indices.

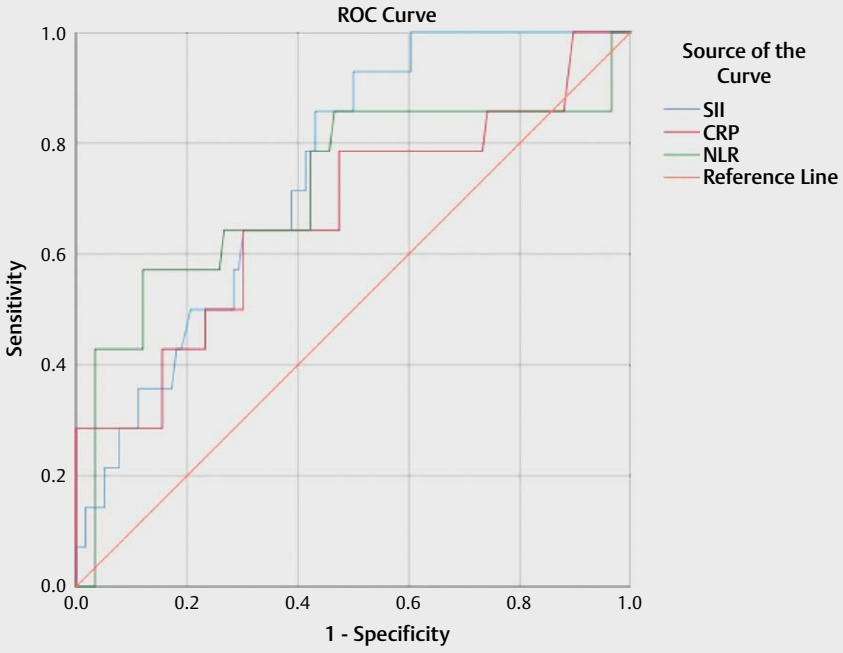
	Sacroiliac joint indices	
	Correlation Coefficient (r)	p-value
C reactive protein	−0.151	0.086
Erithrocyte sedimentation rate	−0.125	0.156
White blood cell count	0.190	0.030
Neutrophil to lymphocyte ratio	−0.057	0.516
Platelet count	−0.019	0.827
Platelet to lymphocyte ratio	−0.271	0.002
Platelet distribution width	−0.140	0.113
Mean platelet value	−0.115	0.194

phil to lymphocyte ratio showed a sensitivity of 64.3 % and specificity of 73.3 % at a cut-off value of 2.32; and C reactive protein showed a sensitivity of 64.3 % and specificity of 69.8 % at a cut-off value of 4.62 mg/L (▶ **Fig. 3**).

Discussion

Inflammatory low back pain with beginning of young adulthood is commonly experienced by patients who have sacroiliitis. Low back pain is one of the most common symptoms in people, and sacroiliitis is not generally considered in differential diagnosis at first. It is difficult to diagnose sacroiliitis at early stages on conventional radiography, and this may lead to a delay of diagnosis by approximately 8 years from onset of symptoms [14–16]. Because of available efficient treatment options, delay of early diagnosis is an unwanted circumstance. Compared to other imaging modalities, MRI has the ability to reveal features of inflammation early, providing shorter delay of diagnosis from onset of symptoms [16, 17]. MRI has been suggested as a modality by ASAS which can be used to evaluate patients for therapeutic perspective. Despite its beneficial effects, MRI has also weaknesses such as cost and availability and contraindications like claustrophobia, metallic implants, and implantable devices [8]. Radionuclide skeletal scintigraphy has the ability to image entire skeleton and joints with high sensitivity at a reasonable cost; it remains widely used despite technological advances in MRI [7]. On the other hand, because of high bone turnover in the region of the sacroiliac region, specificity for diagnosing sacroiliitis is lowered. It is a debate in the literature that whether visual analysis (qualitative) or sacroiliac joint indices (quantitative) findings of radionuclide bone scintigraphy can detect active sacroiliitis. According to the current literature, this is the first study that examines the relationship between the imaging parameters of sacroiliitis and the subclinical inflammation parameters. In our study, there wasn't any correlation between the visual analysis of scintigraphic imaging and subclinical inflammation parameters. On the other hand, a statistically significant correlation was found between active sacroiliitis (bone marrow edema/osteitis) on MRI and subclinical inflammation parameters.

There are few studies in literature specified that bone scintigraphy may be a specific and sensitive method in cases that MRI of the sacroiliac joint is suspiciously negative or MRI cannot be performed [2, 18, 19]. In a study by Song et al. which assess the diagnostic value of scintigraphy for axial spondyloarthritis (SpA) , it was detected that sensitivities of scintigraphy for any (unilateral or bilateral), bilateral and isolated unilateral sacroiliitis were 64.9, 40.2 and 24.7 % and the specificities were 50.5, 57.7 and 92.8 % respectively [18]. In another study by Akdeniz et al. it was also detected that the sensitivities of quantitative scintigraphy and visual scintigraphy were 32 and 82 respectively; the specificity of quantitative scintigraphy were also evaluated as 100 % [19]. The positive predictive values of quantitative scintigraphy and visual scintigraphy were defined as 100 and 92 %, respectively [19]. It was also concluded that regarding MRI as the gold standard in the evaluation of disease activity, combined visual and quantitative bone scintigraphy can be valuable in patients with MRI-incompatible implants in the same study [19]. Kacar et al. was also defined quantitative sacroiliitis scintigraphy as a sensitive tool in diagnosing early sacroiliitis [20]. In our study, a week agreement was detected between MRI and visual scintigraphic analysis for diagnosing active sacroi-



Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95 % Confidence Interval	
				Lower Bound	Upper Bound
SII	0.746	0.057	0.003	0.635	0.858
CRP	0.671	0.085	0.037	0.503	0.838
NLR	0.718	0.088	0.008	0.546	0.890

▶ **Fig. 3** The sensitivity and specificity of inflammation parameters in active sacroiliitis.

liitis. Also significant but weak correlation was detected between MRI and sacroiliac joint indices (quantitative scintigraphic analysis) for diagnosing active sacroiliitis. In our study based on the ROC curve analysis, sacroiliac joint indices revealed a sensitivity of 64.3 % and specificity of 69,8 % at a cut-off value of 1.297. Our findings were not supporting using qualitative or quantitative sacroiliac joint indices if sacroiliac MRI was a readily available option. Also, scintigraphy has a radiation exposure of approximately 4.8 mSv (millisievert) if a standard dosage of about 600 MBq of a Technetium-99 m–labeled radiotracer is used [7] . MRI is convenient from a radiation exposure standpoint and is substantial for early diagnosis of axSpa patients.

Although the pathogenesis of axSpA is controversial, yet some studies have reported the roles of both neutrophils and lymphocytes [21–23]. CBC and its subtypes are known as inflammatory markers in several diseases. Subclinical inflammatory parameters such as neutrophil to lymphocyte ratio has been found to be associated with inflammation in diseases such as Familial Mediterranean Fever [11] . However, the relationships between these subclinical inflammatory parameters and disease activity in axSpA has not been fully understood yet. In some studies, neutrophil to lymphocyte ratio and platelet to lymphocyte ratio were reported to be significantly higher in ankylosing spondylitis (AS) patients with severe disease activity compared to mild disease activity based on BASDAI scores [23–25]. In our study, neutrophil to lymphocyte ratio ($p = 0.008$), C reactive protein ($p = 0.037$), and white blood cell count ($p = 0.031$) were found to be significantly higher in patients with active sacroiliitis compared to patients without active sacroiliitis. Inal et al., Coskun et al., and Kucuk et al. found significant correlation between disease activity (BASDAI scores) and neutrophil to lymphocyte ratio [24–26]. Osami et al., Mercan et al., and Gökmen et al. did not find a significant correlation between BASDAI scores and neutrophil to lymphocyte ratio [23, 27, 28]. Inal et al. reported a significant correlation between BASDAI scores and erythrocyte sedimentation rate and C reactive protein [24] . Osami et al. reported a significant correlation between BASDAI scores and erythrocyte sedimentation rate [23]. A significant correlation was found between active sacroiliitis (bone marrow edema/osteitis) and C reactive protein ($p = 0.000$, $r_{pb} = 0.439$) and erythrocyte sedimentation rate ($p = 0.000$, $r_{pb} = 0.310$) and neutrophil to lymphocyte ratio ($p = 0.001$, $r_{pb} = 0.280$) in our study, congruent with previous studies.

C reactive protein and erythrocyte sedimentation rate are the most widely used laboratory indices for the estimation of AS di-

sease activity [29]. Osami et al. reported erythrocyte sedimentation rate and platelet to lymphocyte ratio as valid fair tests and suggested that neutrophil to lymphocyte ratio has poor validity to differentiate the active AS from inactive AS based on BASDAI scores and sensitivity for erythrocyte sedimentation rate, platelet to lymphocyte ratio, and neutrophil to lymphocyte ratio was 70.9, 70.9, 61.8 % and specificity for erythrocyte sedimentation rate, platelet to lymphocyte ratio, and neutrophil to lymphocyte ratio was 64.9, 55.5, 50.6 %, respectively [23]. Another study reported sensitivity of neutrophil to lymphocyte ratio as 69 % and specificity of 54 % for evaluating disease activity based on BASDAI scores [25]. Additionally, in a study by Huang et al. it was aimed to describe the relationship between the complete blood count parameters and the disease activity of axSpA [30]. The results of this study revealed that neutrophil to lymphocyte ratio and red cell distribution width were both positively correlated with ESR level and CRP level [30]. In the literature, elevated C reactive protein level was suggested as a predictor of radiographic progression [31]. In our study, neutrophil to lymphocyte ratio showed a sensitivity of 64.3 % and specificity of 73.3 %; C reactive protein showed a sensitivity of 64.3 % and specificity of 69.8 % for diagnosing active sacroiliitis (bone marrow edema/osteitis) based on sacroiliac MRI. The laboratory parameters including platelet to lymphocyte ratio, erythrocyte sedimentation rate, white blood cell count, platelet, red cell distribution width and mean platelet value were not found statistically significant at ROC curve analysis. This suggested that neutrophil to lymphocyte ratio together with C reactive protein can be used as potential complementary assessment tools for the diagnosis of disease activity in AS patients. In recent years, acute-phase reactants have been playing a prominent role in monitoring patients with axSpA. The ASDAS is the first validated disease activity score, which combines patient-reported outcomes and CRP or erythrocyte sedimentation rate. ASDAS seems to be a relevant measure to assess disease activity [6, 10]. In this regard, like acute-phase reactants, subclinical inflammation indices obtained from CBC and particularly neutrophil to lymphocyte ratio may have contribution on disease activity assessment. According to these findings, scintigraphy and complete blood count tests can be considered by clinicians when gold standard tests cannot be performed for any reason. However, this needs to be confirmed in further studies

Conflict of Interest

The authors have no potential conflicts of interest to disclose.

References

[1] Slobodin G, Hussein H, Rosner I et al. Sacroiliitis – early diagnosis is key. Journal of inflammation research 2018; 11: 339

[2] Zilber K, Gorenberg M, Rimar D et al. Radionuclide Methods in the Diagnosis of Sacroiliitis in Patients with Spondyloarthritis: An Update. Rambam Maimonides Med J 2016; 7: e0037. doi:10.5041/RMMJ.10264

[3] Lambert RGW, Bakker PAC, van der Heijde D et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. Annals of the Rheumatic Diseases 2016; 75: 1958–1963. doi:10.1136/annrheumdis-2015-208642

[4] Oostveen J, Prevo R. Early detection of sacroiliitis on magnetic resonance imaging and subsequent development of sacroiliitis on plain radiography. A prospective, longitudinal study. The Journal of Rheumatology 1999; 26: 1953–1958

[5] Rudwaleit M, van der Heijde D, Landewé R et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Annals of the Rheumatic Diseases 2009; 68: 777–783. doi:10.1136/ard.2009.108233

[6] van der Heijde D, Ramiro S, Landewé R et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Annals of the rheumatic diseases 2017; 76: 978–991

[7] Song I, Carrasco-Fernandez J, Rudwaleit M et al. The diagnostic value of scintigraphy in assessing sacroiliitis in ankylosing spondylitis: a systematic literature research. Annals of the rheumatic diseases 2008; 67: 1535–1540

[8] Jamar F, Versari A, Galli F et al. Molecular Imaging of Inflammatory Arthritis and Related Disorders. Seminars in Nuclear Medicine 2018; 48: 277–290. doi: https://doi.org/10.1053/j.semnuclmed.2017.12.005

[9] Ziessman HA, O'Malley JP. Nuclear medicine: the requisites E-Book: Elsevier Health Sciences. 2013

[10] van der Heijde D, Lie E, Kvien TK et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Annals of the rheumatic diseases 2009; 68: 1811–1818

[11] Özer S, Yılmaz R, Sönmezgöz E et al. Simple markers for subclinical inflammation in patients with Familial Mediterranean Fever. Medical Science Monitor: İnternational medical journal of experimental and clinical research 2015; 21: 298

[12] Sieper J, Rudwaleit M, Baraliakos X et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Annals of the Rheumatic Diseases 2009; 68: ii1–ii44. doi:10.1136/ard.2008.104018

[13] Fan J, Upadhye S, Worster A. Understanding receiver operating characteristic (ROC) curves. Canadian. Journal of Emergency Medicine 2006; 8: 19–21

[14] Feldtkeller E, Bruckel J, Khan MA. Scientific contributions of ankylosing spondylitis patient advocacy groups Current opinion in rheumatology 2000; 12: 239–247

[15] Spoorenberg A, De Vlam K, Van der Heijde D et al. Radiological scoring methods in ankylosing spondylitis: reliability and sensitivity to change over one year. The Journal of Rheumatology 1999; 26: 997–1002

[16] Heuft-Dorenbosch L, Weijers R, Landewé R et al. Magnetic resonance imaging changes of sacroiliac joints in patients with recent-onset inflammatory back pain: inter-reader reliability and prevalence of abnormalities. Arthritis research & therapy 2005; 8: R11

[17] Rudwaleit M, Van der Heijde D, Khan M et al. How to diagnose axial spondyloarthritis early. Annals of the rheumatic diseases 2004; 63: 535–543

[18] Song I-H, Brandt H, Rudwaleit M et al. Limited diagnostic value of unilateral sacroiliitis in scintigraphy in assessing axial spondyloarthritis. The Journal of rheumatology 2010; 37: 1200–1202

[19] Akdeniz O, Alaylı G, Tosun FC et al. Early spondyloarthropathy: scintigraphic, biological, and clinical findings in MRI-positive patients. Clinical Rheumatology 2008; 27: 469–474. doi:10.1007/s10067-007-0730-y

[20] Kaçar G, Kaçar C, Karayalçin B et al. Quantitative sacroiliac joint scintigraphy in normal subjects and patients with sacroiliitis. Annals of nuclear medicine 1998; 12: 169–173

[21] Braun J, Sieper J. Ankylosing spondylitis. The Lancet 2007; 369: 1379–1390

[22] Bleil J, Maier R, Hempfing A et al. Histomorphologic and histomorphometric characteristics of zygapophyseal joint remodeling in ankylosing spondylitis. Arthritis & Rheumatology 2014; 66: 1745–1754

[23] Al-Osami MH, Awadh NI, Khalid KB et al. Neutrophil/lymphocyte and platelet/lymphocyte ratios as potential markers of disease activity in patients with Ankylosing spondylitis: a case-control study. Advances in Rheumatology. 2020; 60

[24] İnal EE, Sunar I, Sarataş Ş et al. May neutrophil-lymphocyte and platelet-lymphocyte ratios indicate disease activity in ankylosing spondylitis? Archives of rheumatology 2015; 30: 130–137

[25] Kucuk A, Uslu A, Ugan Y et al. Neutrophil-to-lymphocyte ratio is involved in the severity of ankylosing spondylitis. Bratislavske lekarske listy 2015; 116: 722–725

[26] Coşkun BN, Öksüz MF, Ermurat S et al. Neutrophil lymphocyte ratio can be a valuable marker in defining disease activity in patients who have started anti-tumor necrosis factor (TNF) drugs for ankylosing spondylitis. European journal of rheumatology 2014; 1: 101

[27] Gökmen F, Akbal A, Reşorlu H et al. Neutrophil–lymphocyte ratio connected to treatment options and inflammation markers of ankylosing spondylitis. Journal of clinical laboratory analysis 2015; 29: 294–298

[28] Mercan R, Bitik B, Tufan A et al. The association between neutrophil/lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis. Journal of clinical laboratory analysis 2016; 30: 597–601

[29] McVeigh CM, Cairns AP. Diagnosis and management of ankylosing spondylitis. Bmj 2006; 333: 581–585

[30] Huang Y, Deng W, Zheng S et al. Relationship between monocytes to lymphocytes ratio and axial spondyloarthritis. International immunopharmacology 2018; 57: 43–46

[31] Poddubnyy D, Haibel H, Listing J et al. Baseline radiographic damage, elevated acute-phase reactant levels, and cigarette smoking status predict spinal radiographic progression in early axial spondylarthritis. Arthritis & Rheumatism 2012; 64: 1388–1398